Level of evidence supporting the Chinese cardiovascular disease clinical practice guidelines and its evolution in the past two decades

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Summary

Background Clinical practice is guided by guidelines in the era of evidence-based medicine to improve healthcare. The consistency between the strength of recommendations and the underlying quality of evidence in clinical guidelines and its evolution dynamically reflects the status of medical practice in important aspects. This study aimed to evaluate the levels of evidence (LOEs) supporting different classes of recommendations (CORs) in Chinese cardiovascular disease (CVD) guidelines between 2003 and 2021, and changes over time.

Methods Clinical guideline documents on cardiovascular topics issued by leading professional organizations were retrieved in the Databases of SinoMed and Wanfang Med Online from inception to June 2021. All guidelines were screened through abstract and full-text reading, and included if satisfying the pre-specified criteria. 79 Chinese guideline documents on 12 sub-topics including a total of 5195 recommendations and the designated CORs/LOEs, were abstracted. The number of recommendations of Class I, Class II, Class III, LOE A, LOE B, and LOE C were identified for each guideline document. The proportion of CORs, LOEs, and COR-LOE combinations in guidelines and the changes among those with ≥2 versions.

Findings A total of 79 guidelines were included in the analysis. When examining the status of current guidelines, among the 3325 recommendations derived from 59 documents during 2011–2021, 735 recommendations (22.1%) were classified as LOE A, 1280 (38.5%) as LOE B, and 1310 (39.4%) as LOE C. 596 recommendations (17.9%) were characterized as Class I-LOE A, accounting for the majority of LOE A recommendations but only one-third of Class I recommendations. Evidence levels varied greatly across different sub-topics and individual guidelines. There are 9 guidelines on 5 sub-topics having ≥2 versions. When analyzing the changes over time, although an increase was observed in the total number of recommendations, the proportion of recommendations designated as Class I-LOE A did not significantly improve (19.1% [current] vs 19.0% [prior], $p = 0.97$).

Interpretation In current Chinese CVD guidelines, the high level of evidence lacks, and its alignment with strong recommendations is deficient. Although it shows moderate improvements in certain major topics (e.g., coronary artery disease, interventional therapy, surgery) in the past two decades, the overall proportion of Class I-LOE A recommendations remains small, suggesting that conduction, and particularly translation, of high-quality studies like RCTs addressing CVDs-related questions are still essential and demanded, especially for areas with less attention.

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Research in context

Evidence before this study

The quality of evidence underlying the guideline recommendations is critical, and the alignment of strong recommendation with high-quality evidence is the key to the trustworthy guidelines. Several studies have evaluated the level of evidence supporting the European Society of Cardiology and American College of Cardiology/American Heart Association guidelines. However, the evidence foundation of Chinese cardiovascular guidelines has not been fully studied, which has an important impact on a large volume of patients in China.

Added value of this study

In this study, a total of 79 guidelines including 5195 recommendations were analyzed. When examining the current guidelines, the proportion of recommendations supported by level A of evidence (LOE) varied greatly across guidelines of different sub-topics, ranging from 2.4% to 46.9%. A significant discordance between strong recommendations and high-quality evidence was observed, with a proportion of 22.1% for LOE A, while 53.7% for Class I recommendation. Furthermore, less than 20% recommendations were classified as Class I-LOE A. Over the past two decades, the overall proportion of Class I-LOE A recommendations remained at a similarly low level, which is particularly substantial in some understudied topics.

Implications of all the available evidence

In Chinese CVD guidelines, there is a lack of high-level evidence and a remarkable discordance between strong recommendations and high-quality evidence. Our findings suggest that the considerable gaps in conclusive evidence underlying the Chinese CVD guidelines are required to fill in by improving the quantity and quality of cardiovascular research, and fostering the translation of RCT results into solid evidence, especially for the areas with less attention.

Introduction

Clinical practice guidelines support the clinical decisions (e.g., treatments) of healthcare practitioners, and assist in improving the quality of medical service and patients' prognosis.[1,2] Experts from academic organizations systematically review clinical research evidence, and carefully develop such guidelines by making recommendations of different strengths. Considering medical advances and updates of the evidence, guidelines are revised periodically. Cardiovascular clinical guidelines play an important role in the care of patients with cardiovascular disease (CVD), which is the leading death cause worldwide.[3,4] However, in a recent systematic review of American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) guidelines, only less than 10% of ACC/AHA and 15% of ESC recommendations are supported by level A of evidence (LOE), which is defined as the highest evidence level from multiple randomized controlled trials (RCTs) or meta-analysis based on RCTs.[5] Moreover, the pattern of a small proportion of recommendations that were LOE A has not shown significant improvement over time.[5,6]

In China, the incidence and fatality rates of CVDs have been rising year by year.[7] Similarly, to provide appropriate healthcare and make optimal clinical decisions, Chinese guidelines for CVDs have been developed since 1992, mainly by the subordinate societies or associations of the Chinese Medical Association (CMA), the Chinese Medical Doctor Association (CMDA), and the National Health Commission of the People's Republic of China (NHC). With the continuous development of evidence-based medicine in China, various types of studies including RCTs on CVDs conducted among Chinese people are also growing rapidly, therefore expecting a great amount of evidence, particularly high quality evidence, available for issuing recommendations.[8] Yet, the alignment of strength of recommendations with the underlying quality of evidence in Chinese CVD guidelines, and how the alignment changes in the past two decades remain unclear. By describing the classes of recommendations (CORs) and LOEs in current guidelines, our study aims to elucidate the regional characteristics of these evidence-based documents and potential gaps compared with western countries. In addition, whether the substantial increase in research among the Chinese population has provided more conclusive evidence, and truly addressed more unresolved issues remains unknown. Therefore, our study also investigates the temporal changes of the underlying evidence in Chinese cardiovascular guidelines over approximately 20 years. Considering the rapid progress of clinical research in the cardiovascular field in China, the huge volume of patients,[4,8] and most importantly, the wider application of Chinese guidelines especially among the local physicians from low-level hospitals, this study will have a huge impact on clinical practice in China and is of great value for the future research directions. In addition, the development of cardiovascular guidelines in China is not initiated by a

specific academic organization like ACC/AHA and ESC but involves multiple societies or associations, which also makes this study with regional characteristics.

Methods

Unlike ACC/AHA and ESC guidelines, Chinese clinical practice guidelines for CVDs are not accessible on a fixed website as they are released by multiple subordinate societies or associations. Instead, they are usually published in different Chinese academic journals. Therefore, we did a systematic search using the Chinese Biomedical Database (also known as SinoMed, http://www.sinomed.ac.cn/) and Wanfang Med Database (http://med.wanfangdata.com.cn/), two main medical databases in China, until June 2021. The keywords and search strategies used were presented in the Supplements.

All guidelines providing explicit classes of recommendation (CORs) and LOEs are included, without restrictions on the date of issue. To enhance the comparability with AHA/ACC or ESC guidelines, those using the same or similar grading schema, which is based on the CORs (I/II/III) and LOEs (A/B/C), were deemed as eligible. In addition, considering a proportion of Chinese guiding documents were issued under the category of expert consensus, they were also included if the recommendations were developed in the same way as above in the conventional "Guidelines", and CORs and LOEs were provided. The guidelines using the GRADE system, the interpretations, comments as well as translation of European and American guidelines were excluded. Titles and abstracts were initially reviewed and all related records were further evaluated by full-text review to determine the eligibility. The screening process was performed independently by 2 authors (C.L. and C.S.W.) and any discrepancy was resolved by a third senior author (Y.D.T.). The process of literature retrieval and screening was depicted in Fig. 1. The detailed information of all included guidelines and their DOIs were summarized in the Supplements. In this analysis, each guideline has at most 3 versions, which are discriminated against by the corresponding issued years and classified as versions of "earliest", "prior", and "current". In addition, 10-year was selected as a cycle based on previous studies,[5,9] with the period of 2011–2021 specified as the current cycle. From year 2000, the earliest eligible guideline was issued in 2003, and therefore was set as the beginning of this analysis.

The two authors independently counted and recorded the number of recommendations (composed of one or a few sentences), the classes and levels of supporting evidence, and discussed any discrepancy with a third senior author. Consistent with AHA/ACC and ESC guidelines, the definitions of CORs and LOEs are as follows: Class I: recommendation refers to the proven or unanimously recognized beneficial or effective procedure or treatment. Class II: including class IIa recommendation, of which procedure or treatment is likely to be effective with some controversy suggested by the existing evidence or views; and class IIb recommendation, for which, the effectiveness of the procedure or treatment cannot be fully proven by the existing evidence. Class III: recommendation refers to the proven or unanimously recognized ineffective procedure or treatment. The level of supporting evidence is divided into three categories: LOE A refers to the evidence from multiple RCTs or their meta-analysis. LOE B refers to evidence from single RCT or large-scale non-RCTs. LOE C refers to evidence from expert opinions or consensus, small-scale or retrospective studies, etc.

Data extraction and analysis

The number of recommendations by classes and LOEs from individual guidelines was abstracted. All included guidelines on various subjects were divided into 5 categories and 12 sub-topics: disease-based (coronary artery disease (CAD), heart failure, hypertension, arrhythmias, pulmonary hypertension, cardiomyopathy, cardiometabolic diseases), procedure-based (interventional therapy, surgery), prevention-based (prevention), diagnosis-based (diagnosis), and others (eTable S1). To describe the evolution of CVD guidelines in China, we first examined the distribution of recommendations and the underlying evidence foundation of current guidelines, which were defined as the latest published version. However, considering the significant updates of scientific research that occurred as well as technical and medical development recently, current guidelines issued in the last decade (2011–2021) were selected for analysis of the current status. The number and percentage of recommendations were reported by sub-topics. Further, we analyzed the changes in the recommendations from the guidelines with ≥2 versions by comparing the current version to its previous one. Heat maps and line plots were used to illustrate the changes in CORs and LOEs. Changes in the proportion of Class I-LOE A (I-A) recommendations were also computed. In addition, the chi-square test was applied to compare the distribution of guideline recommendations of varying COR-LOE combinations for the periods of 2003–2010 and 2011–2021. All statistical analyses were performed using SAS (version 9.4) or R software (version 4.0.5).

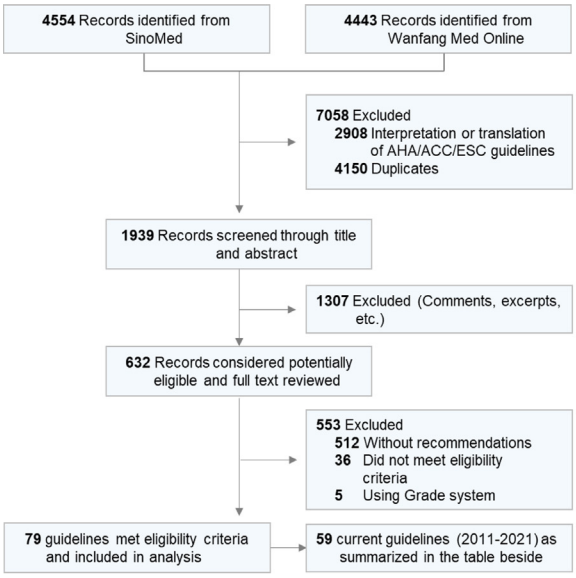
Role of the funding source

The funders played no role in the study design, data collection, data analysis, interpretation or writing of this report.

Results

Historical and current summary

As of 2003, when the first guideline using the COR- and LOE-based grading scheme was released, the number of



59 Current Guidelines (2011-2021)

Category	Sub-Topic	Number
Disease-based	Coronary Artery Disease	10
	Heart Failure	6
	Hypertension	4
	Arrythmia	4
	Pulmonary Hypertension	4
	Cardiomyopathy	3
	Cardiometabolic Disease	2
Procedure-based	Interventional Therapy	5
	Surgery	12
Prevention-based	Prevention	3
Diagnosis-based	Diagnosis	3
Others	Others	3
Total		59

Fig. 1: **Literature retrieval and screening process.** Abbreviations: AHA, American Heart Association; ACC, American College of Cardiology; ESC, European Society of Cardiology.

guidelines showed an increasing trend overall, and had significant increases in 2016 and 2020 (eFigure S1a). Data from a total of 79 guidelines including 5195 recommendations were abstracted. Among them, there were 48 disease-based, 20 surgical/interventional procedure-based, 3 prevention-based, and 3 diagnosis-based guidelines, respectively (eTable S1). It is worth noting that guidelines in the categories of procedure, prevention, and diagnosis were mainly issued in 2020, leading to explosive growth. When analyzed by sub-topics, CAD accounts for the largest proportion, with 17 issued guidelines (21.5%) related to 10 subjects, followed by surgery (12, 15.2%), and heart failure (10, 12.7%), as shown in eTable S1. There were 5 associations/societies issuing ≥5 guidelines (eFigure S1b). To be specific, the Chinese Society of Cardiology (CSC) has released the most guidelines (n = 37), making up nearly half of all documents. The National Center for Cardiovascular Diseases (NCCD) and the Chinese College of Cardiovascular Physicians (CCCP) are involved in developing 11 and 10 guidelines, respectively.

Current status

There are 59 documents deemed as the current guidelines in the past decade, including 3325 recommendations. Of which, more than half (n = 1785) were characterized as Class I ("should do"), and approximately 5% (n = 164) as Class III ("should not do"). By contrast, only 22% (n = 735) of recommendations were classified as LOE A and nearly 40% (n = 1310) as LOE C (Table 1). When analyzed by sub-topics, the distribution of CORs and LOEs varied greatly. Despite the fewest recommendations, cardiometabolic disease had the most percentage of LOE A, more than twice the overall average. The proportion of Class I/III was similarly higher than the remaining sub-topics. Interventional therapy also included a moderate higher proportion of Class I/III and LOE A recommendations. While for pulmonary hypertension and cardiomyopathy, it showed that 70.5%, and 64.5% of recommendations were classified as LOE C, ranking the top two with significantly lower proportions of LOE A. The number of recommendations for CAD was the largest, accounting for more than one-fifth of all sub-topics. It had >60% of Class I/III recommendations but less than 30% were made based on LOE A. Compared with recommendations supported by LOE B, the proportion of LOE A recommendations showed greater variation, ranging from 2.4% to 46.9%.

When examining the proportion of recommendations by classes and evidence levels, Class I consisted of similar proportions of recommendations supported by LOE A, B, and C (Fig. 2). Within the Class II recommendations, the proportions of LOE B and LOE C were substantially higher than that of LOE A. While Class III included the lowest proportion of recommendations stemming from the evidence of different levels, with 1.1%, 1.7%, and 2.2% for LOE A, B, and C, respectively (eTable S2). As for the I-A recommendation, the percentage of which was highest (44.4%) in the subtopic of cardiometabolic disease, followed by intervention therapy at 27.8%, hypertension at 25.8%, and diagnosis at

Sub-topics (No[b])	Class of recommendation/level of evidence, No.[a] (%)						
	Class I	Class II	Class III	A	B	C	Total
Coronary artery disease (n = 10)	431 (57.0)	286 (37.8)	39 (5.2)	221 (29.2)	296 (39.2)	239 (31.6)	756
Heart failure (n = 6)	256 (54.9)	190 (40.8)	20 (4.3)	99 (21.2)	145 (31.1)	222 (47.6)	466
Hypertension (n = 4)	141 (53.4)	112 (42.4)	11 (4.2)	77 (29.2)	82 (31.1)	105 (39.8)	264
Arrythmia (n = 4)	200 (49.5)	176 (43.6)	28 (6.9)	68 (16.8)	219 (54.2)	117 (29.0)	404
Pulmonary hypertension (n = 4)	97 (58.4)	58 (34.9)	11 (6.6)	17 (10.2)	32 (19.3)	117 (70.5)	166
Cardiomyopathy (n = 3)	109 (43.4)	129 (51.4)	13 (5.2)	6 (2.4)	83 (33.1)	162 (64.5)	251
Cardiometabolic disease (n = 2)	55 (67.9)	20 (24.7)	6 (7.4)	38 (46.9)	25 (30.9)	18 (22.2)	81
Interventional therapy (n = 5)	116 (58.6)	71 (35.9)	11 (5.6)	69 (34.8)	58 (29.3)	71 (35.9)	198
Surgery (n = 12)	123 (41.4)	173 (58.2)	1 (0.3)	27 (9.1)	141 (47.5)	129 (43.4)	297
Prevention (n = 3)	71 (56.8)	42 (33.6)	12 (9.6)	33 (26.4)	68 (54.4)	24 (19.2)	125
Diagnosis (n = 3)	140 (56.2)	99 (39.8)	10 (4.0)	75 (30.1)	105 (42.2)	69 (27.7)	249
Others (n = 3)	46 (67.6)	20 (29.4)	2 (2.9)	5 (7.4)	26 (38.2)	37 (54.4)	68
Total (n = 59)	1785 (53.7)	1376 (41.4)	164 (4.9)	735 (22.1)	1280 (38.5)	1310 (39.4)	3325
Summary of all guidelines median (IQR)%	56.5 (51.5–58.5)	38.8 (34.3–43.0)	5.2 (4.1–6.8)	23.8 (9.7–29.7)	35.7 (31.0–44.9)	37.9 (28.4–51.0)	

Abbreviation: IQR, interquartile range. [a]Refers to the number of recommendations in guidelines. [b]Refers to the number of guidelines in each sub-topic.

Table 1: **Distribution of recommendation class and level of evidence in current guidelines.**

25.3%. The lowest proportion of I-A was in cardiomyopathy with 6 (2.4%) recommendations (eTable S2).

Changes over time

Only 9 of 79 guidelines from 5 sub-topics were periodically updated (eTable S3). Of those, 5 subjects had one previous version, and 4 subjects, including pulmonary hypertension, ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation acute coronary syndrome (NSTE-ACS), and percutaneous coronary intervention (PCI), had 3 versions of the earliest, the prior, the current. The median update period was 4 years (interquartile range [IQR]: 3–4). In contrast, guidelines for supraventricular arrhythmia as well as pacemaker, and implantable cardioverter-defibrillator have not been revised for more than 10 years.

Among guidelines with ≥2 updates, there were 5 subjects (ventricular arrhythmia, medication for heart failure, STEMI, pulmonary hypertension, and ACS) for which an increase in the number of recommendations

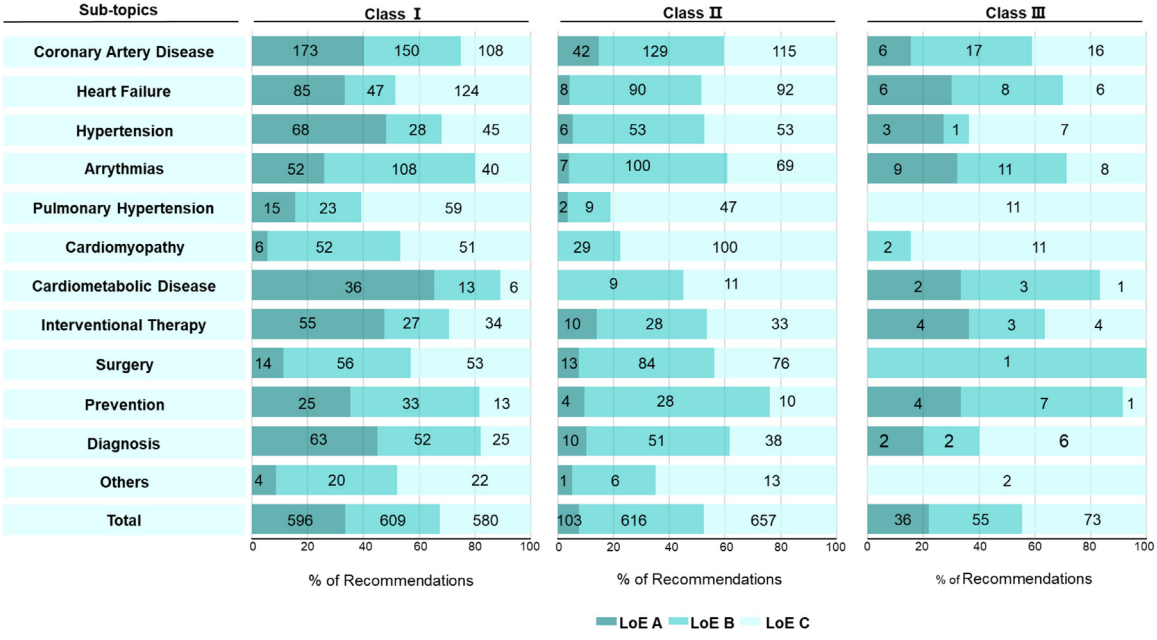


Fig. 2: **Distribution of level of evidence by recommendation class in current guidelines.** Numbers within each column of the chart represent the absolute number of recommendations. Abbreviation: LoE, level of evidence.

was observed in the current document in comparison to the prior one. Whereas guidelines of the rest 4 subjects saw a reduction, especially for NSTE-ACS and PCI (Fig. 3a and eTable S4). Regarding the Class I recommendations, the proportion in guidelines for ACS, medication of CAD, pulmonary hypertension, and PCI substantially increased by about 10% or higher. The proportion of recommendations supported by LOE A rose continuously for STEMI and PCI. The percentage of I-A recommendations observed similar changes. Additionally, the proportion of lowest evidence level in medication of CAD and ventricular arrhythmia markedly dropped by more than 20% (Fig. 4; eTable S5). Overall, compared with the prior version, although the number of recommendations supported by LOE A increased from 256 to 324, the proportion of LOE A remained virtually unchanged (24.2% vs 24.1%) due to the growth of total recommendations (Fig. 3b). It showed similar results for the proportion of I-A recommendations (19.1% vs 19.0%).

In addition, we examined the change in the distribution of recommendations of different COR-LOE combinations between the periods of 2003–2010 and 2011–2021 (Table 2). It showed no significant change in the proportions of recommendations within any Class I-LOE or COR-LOE A combinations. By contrast, there was substantial changes in the proportion for the remaining combinations, with the largest absolute increase observed in II-B (+5.5%) and decrease in III-C (−3.6%).

Discussion

In this study, we summarized and analyzed the CVD guidelines released by Chinese societies or associations from 2003 to 2021, and focuses on the LOEs underlying the current guideline recommendations in the past decade and the changes over time. In current guidelines, it was found that the proportion of LOE A recommendations was only 22.1% and 67.6% of Class I and III recommendations (highly recommended or not) were not supported by LOE A, reflecting a less certain level of evidence for recommendations of higher strength. Furthermore, the percentage of LOE A recommendations varied greatly across sub-topics, which was as high as 46.9% in cardiometabolic disease but only 2.4% in cardiomyopathy. An increase in the proportion of LOE A recommendations was observed in some subjects than the prior ones, although the overall proportion has not improved significantly, which indicated that the evidence foundation in some disease areas has made noticeable progress. Our findings suggested the considerable gaps in conclusive evidence of CVD clinical practice required to fill in, and limited translation of RCT findings into solid evidence.

Our study reported a higher number and proportion of recommendations characterized as LOE A in current Chinese CVD guidelines (735, 22.1%) compared with the ACC/AHA (248, 8.5%), and ESC (484, 14.2%) guidelines,[5] the established guidance for CVDs in western countries. This observed difference in the number of recommendations characterized as LOE A across the current guidelines is possibly due to the discrepancy in the analyzed guidelines, and the substantial increase in the number of clinical research related to CVDs in China. In 2019, Fanaroff et al. reported the abovementioned data by analyzing ACC/AHA and ESC guidelines released from 2008 to 2018,[5] which is not completely consistent with the period

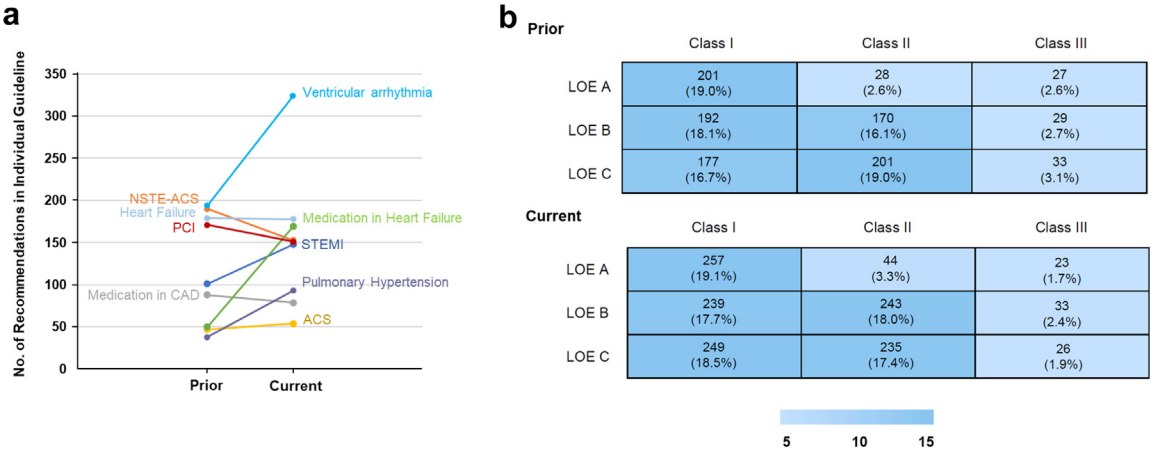


***Fig. 3:* Comparison of recommendations by classes and evidence levels between prior and current guideline documents.** (a) Line plot: the change in the total number of recommendations from the prior guidelines to the current ones; (b) Heat map: the comparison of distribution of recommendations between the prior and current guidelines. Abbreviations: NSTE-ACS, non-ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; CAD, coronary artery disease; STEMI, ST-segment elevation myocardial infarction; ACS, acute coronary syndrome; LoE, level of evidence.

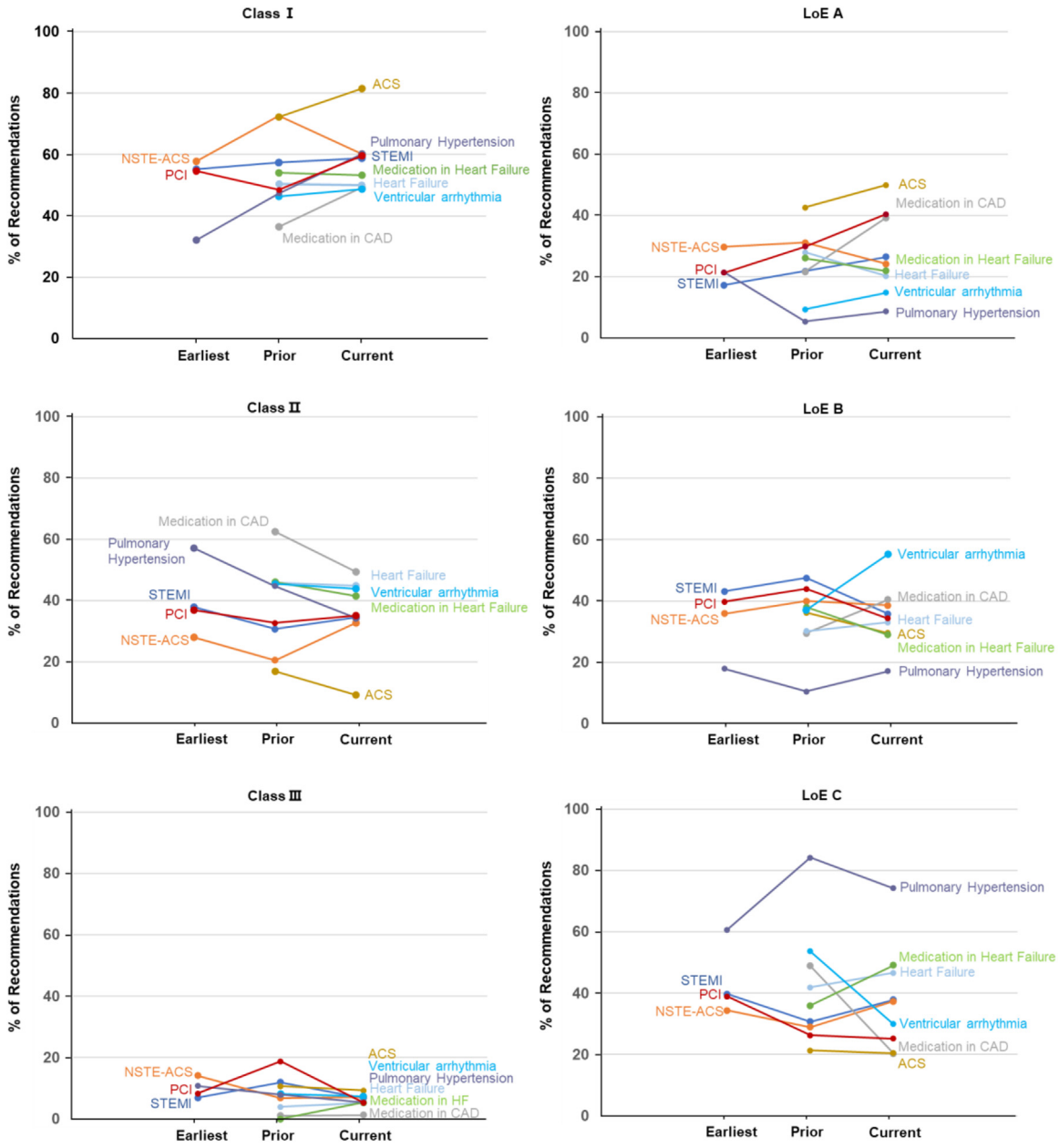


Fig. 4: **The proportion of recommendations by classes and evidence levels in the earliest, prior, and current guideline documents.** Abbreviations: NSTE-ACS, non-ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; CAD, coronary artery disease; STEMI, ST-segment elevation myocardial infarction; ACS, acute coronary syndrome; LoE, level of evidence.

(2011–2021) analyzed in our study. There were 43% of current guidelines (34 of 59) published during 2019–2021 in our analysis. On the other hand, the Chinese government, institutions, and health professionals have made tremendous efforts to improve the prevention and management of CVDs.[8] In the cardiovascular field, the research funding support from the government (e.g., Natural Science Foundation of China) and industry has increased dramatically in the past decade, contributing to the rapid development of cardiovascular research.[8] Moreover, the increasing number of registered trials, especially RCTs with significant impacts (e.g., BRIGHT trial),[10] and scientific papers related to CVDs facilitate making recommendations with more definitive evidence.[8,11] In addition, encouragingly, with the heightened awareness of the great

Period	No. of guidelines	Class of recommendation/level of evidence, No.[a] (%)									
		I-A	I-B	I-C	II-A	II-B	II-C	III-A	III-B	III-C	Total
2003–2010	11	125 (15.4)	141 (17.4)	136 (16.7)	32 (3.9)	106 (13.1)	189 (23.3)	12 (1.5)	24 (3.0)	47 (5.8)	812
2011–2021	59	596 (17.9)	609 (18.3)	580 (17.4)	103 (3.1)	616 (18.5)	657 (19.8)	36 (1.1)	55 (1.7)	73 (2.2)	3325
Change, %		2.5	1.0	0.7	−0.8	5.5	−3.5	−0.4	−1.3	−3.6	NA
p value		0.0883	0.5282	0.6389	0.2254	0.0002	0.0259	0.3459	0.0151	<0.0001	NA

For each period, only guidelines of the latest version were included for analysis. Abbreviation: NA, not applicable. [a]Refers to the number of recommendations in guidelines.

Table 2: **Recommendations within each class of recommendation-level of evidence combination in different periods.**

value of clinical research, the quantity of high-quality RCTs led by and conducted among the Chinese like the FAVOR III China trial,[12] and the STEP trial[13] is continuously on the rise, providing more effective strategies with solid evidence for cardiac practice in the future. Yet, the absence of a specific methodology manual for Chinese guidelines may also bring divergences. Given the importance of guidelines, these documents are supposed to be created with a rigorous methodology. To assist guideline writers in crafting recommendations, the ACCF/AHA Task Force on Practice Guidelines has created a methodology manual for guidelines on diverse topics.[14] Nevertheless, most Chinese CVD guidelines only briefly depicted the process of development and the grading schema in a few sentences, which makes it less transparent and challenging to evaluate the methodological rigor. Besides, our study observed a similarly high proportion of strong recommendations (i.e., Class I or III) that were not characterized as LOE A with ACC/AHA and ESC guidelines, which further indicated the inadequacy of high certainty evidence underlying the current recommendations. It is reported that less than 1% of papers on CVDs led by Chinese authors were published in the top cardiovascular journals in 2017,[8] suggesting a paucity of research quality. Therefore, despite the efforts from all stakeholders in the cardiovascular field and the progress achieved in China, enhancing research quality and translation of findings from high-quality research into effective clinical strategies still have a long way to go.

When analyzing by sub-topics, a wide variation in the levels of supporting evidence across current guidelines was observed. The lack of LOE A for the recommended actions was most obvious for guidelines like cardiomyopathy, with only 6 LOE A recommendations but including more than 60% LOE C recommendations. A similar pattern of the underlying evidence was seen for pulmonary hypertension, likely explained by the complexity of the disease and the difficulty in recruiting patients. Our results pointed to the weak evidence-based foundation dominated by expert opinions, and emphasized the necessity of putting more effort into conducting well-designed research in these fields, such as by strengthening the multicenter collaboration. In addition, as for surgery, a series of guidelines related to congenital heart diseases have been released in 2020, and yet had a small proportion of LOE A recommendations. The lack of evidence from RCTs supporting surgical procedures in our study was consistent with results reported by a recent study.[15] It is believed that additional challenges exist for conducting cardiac surgery RCTs, from trial design, implementation to analysis, when compared to nonsurgical trials.[15,16] Gaudino et al. discussed these issues, and provided a list of suggestions to take.[15] By contrast, owing to the large volume of patients in the areas of CAD, heart failure, hypertension, and cardiometabolic disease, the funding support for the RCTs of relevant treatments (drugs or devices) in those fields is substantial, resulting in the average high proportion of LOE A recommendations. Besides, it is noteworthy that there are two guidelines related to Traditional Chinese Medicine (TCM) under the subspecialty of CAD, despite the relatively low percentage of LOE A recommendations. From a historical perspective, TCM has been playing a crucial function in clinical practice in China, and the related research gets comprehensive support from the Chinese government, aiming to promote its development. Several RCTs have shown that TCM could be a supplementary treatment to combat CVDs.[17,18] Yet, there is much room for improvement, and a boost is anticipated in both the quantity and the quality of clinical studies regarding TCM in the cardiovascular field with efforts from all parties involved. On top of that, increasing attention has been paid to the prevention of CVDs, while there is a lack of guidelines in certain areas such as myocarditis and Kawasaki disease in China.

As for the evolution during the past two decades, the overall proportion of LOE A recommendations did not show a meaningful change between the prior and the current guidelines. By contrast, a slight decrease has been previously reported for ACC/AHA and ESC guidelines.[5] Similar results for LOE A recommendations were observed when comparing the guidelines issued during 2003–2010 with those during 2011–2021. These data showed that the quantity of definitive evidence underlying the Chinese guideline recommendations did not increase. Despite the substantial increase in scientific research, the evidence-based foundation remained weak. As pointed out in the study of Tricoci and

colleagues,[6] numerous studies were driven by industry, aiming to obtain regulatory approval of new drugs or devices instead of addressing unresolved practical clinical issues. Therefore, it is of great importance to increase the funding support from non-profit organizations for research answering clinical practice questions to help generate the evidence required in weighing benefits and risks. On the other hand, encouragingly, it had increases in the proportion of LOE A recommendations in some subjects, reflecting the improved evidence foundation in certain fields, like PCI.

The Chinese cardiovascular guidelines dated back to 1992, with the earliest one related to the pacemaker released, while the first guideline providing definite recommendations with designated classes and LOEs was issued in 2003. Although an increasing number of Chinese CVD guidelines incorporate specific designations in recommendations, there were still many guidelines not. Moreover, the absence of definite sources of evidence in quite a few guideline recommendations impaired the reliability. The Chinese CVD guidelines are published in different Chinese journals, which limits potential international communications, and make it inconvenient to obtain all issued documents. The CMA just established the CMA journal database (http://www.yiigle.com), which collects all the guidelines released by itself. Yet the collection is found incomplete and lacked some historical guidelines, which is expected to be continuously improved. Compared with the guidelines of ACC/AHA and ESC, the subjects of the Chinese guidelines were too subdivided, and it lacks periodic updates in multiple guidelines, impeding the translation of the latest RCT findings into guideline recommendations. The present format of Chinese guidelines also needs improvements given that such lengthy documents without a separate list or table summarizing the recommendations likely hinder the health professionals from efficiently obtaining instructive information.

Implications

Our study showed that the high level of evidence underlying the current Chinese CVD guidelines was insufficient, and it did not change meaningfully compared with the prior ones. The evidence-based foundation needs to be continuously strengthened by improving the quality of research, and fostering the translation of RCT findings into effective strategies. Furthermore, more continuous support (e.g., funding, resources) should be focused on high-quality research addressing practical clinical questions. Moreover, regarding the guideline development and writing, the creation of a rigorous methodology manual, and the adoption of a standardized presenting format are highly recommended. With the tremendous efforts from all stakeholders, including government, industry, and individuals, considering the population base and the current state of cardiovascular research in China, it is anticipated that the Chinese cardiovascular clinical guidelines will have a highly positive impact on global cardiovascular health in the future.

Limitations

There are several limitations in this study. First, the guidelines based on the GRADE system were excluded to enhance the comparison with AHA/ACC or ESC guidelines, although it is one of the commonly used evidence classification systems worldwide. The exclusion may partially affect the comprehensiveness of the analysis. Second, the quality of evidence underlying the guideline recommendations analyzed in our study was directly abstracted from the guideline documents instead of being reassessed by ourselves. The lack of detailed description of the development process in many guidelines, and the potential changes of guideline writing committee over time could influence the evidence level designations. Third, the quality evaluation of guidelines was not performed in this study, which is also an important research direction for evidence-based evaluation of Chinese cardiovascular guidelines in the future. Fourth, the guidelines on cerebrovascular diseases such as stroke, which were developed by the societies of neurology and neurosurgery, were removed from the present study. Therefore, the results in our study cannot reflect the quality of evidence in this field.

Conclusion

There is a lack of high level of evidence in Chinese CVD clinical guidelines, and the alignment of strong recommendations with the underlying high-quality evidence is deficient, with only one-third of Class I recommendations supported by LOE A. Although it shows moderate improvements in certain major topics in the past two decades, the overall proportion of Class I-LOE A recommendations remains small, suggesting that conduction, and particularly translation, of high-quality studies like RCTs addressing CVDs-related questions are still essential and demanded, especially for areas with less attention.

Contributors

C.L. and C.S.W.: conceptualisation, methodology, guideline screening, data collection, statistical analysis, and manuscript writing.

J.H.: data analysis.

Y.T.Z., J.Y., and W.Y.W.: technical support, suggestion, and revision.

Y.D.T.: supervision, professional suggestion, and revision.

Data sharing statement

The data used and analyzed in this study are available from the corresponding author with reasonable request.

Declaration of interests

All authors declared no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100773.

References

1 Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. *JAMA*. 1992;268(17):2420–2425.
2 Shortell SM, Rundall TG, Hsu J. Improving patient care by linking evidence-based medicine and evidence-based management. *JAMA*. 2007;298(6):673–676.
3 GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease study 2019. *Lancet*. 2020;396(10258):1204–1222.
4 Liu S, Li Y, Zeng X, et al. Burden of cardiovascular diseases in China, 1990-2016: findings from the 2016 Global Burden of Disease study. *JAMA Cardiol*. 2019;4(4):342–352.
5 Fanaroff AC, Califf RM, Windecker S, Smith SC Jr, Lopes RD. Levels of evidence supporting American College of Cardiology/American Heart Association and European Society of Cardiology guidelines, 2008-2018. *JAMA*. 2019;321(11):1069–1080.
6 Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines. *JAMA*. 2009;301(8):831–841.
7 Du X, Patel A, Anderson CS, Dong J, Ma C. Epidemiology of cardiovascular disease in China and opportunities for improvement: JACC International. *J Am Coll Cardiol*. 2019;73(24):3135–3147.
8 Liu J, Ma C. Current state of cardiovascular research in China. *Nat Rev Cardiol*. 2019;16(10):575–576.
9 DuBose-Briski V, Yao X, Dunlay SM, et al. Evolution of the American College of Cardiology and American Heart Association Cardiology clinical practice guidelines: a 10-year assessment. *J Am Heart Assoc*. 2019;8(19):e012065.
10 Han Y, Guo J, Zheng Y, et al. Bivalirudin vs heparin with or without tirofiban during primary percutaneous coronary intervention in acute myocardial infarction: the BRIGHT randomized clinical trial. *JAMA*. 2015;313(13):1336–1346.
11 Hu X, Yang HT, Zhu Y, Wang J, Dong E. Chinese basic cardiovascular research in transition. *Circ Res*. 2016;118(12):1876–1879.
12 Xu B, Tu S, Song L, et al. Angiographic quantitative flow ratio-guided coronary intervention (FAVOR III China): a multicentre, randomised, sham-controlled trial. *Lancet*. 2021;398(10317):2149–2159.
13 Zhang W, Zhang S, Deng Y, et al. Trial of intensive blood-pressure control in older patients with hypertension. *N Engl J Med*. 2021;385(14):1268–1279.
14 Methodologies and policies from the ACCF/AHA Task Force on practice guidelines. 2010. https://professional.heart.org/en/guidelines-and-statements/methodologies. Accessed April 25, 2023.
15 Gaudino M, Kappetein AP, Di Franco A, et al. Randomized trials in cardiac surgery: JACC review topic of the week. *J Am Coll Cardiol*. 2020;75(13):1593–1604.
16 Gaudino M, Chikwe J, Bagiella E, et al. Methodological standards for the design, implementation, and analysis of randomized trials in cardiac surgery: a scientific statement from the American Heart Association. *Circulation*. 2022;145(4):e129–e142.
17 Li X, Zhang J, Huang J, et al. A multicenter, randomized, double-blind, parallel-group, placebo-controlled study of the effects of qili qiangxin capsules in patients with chronic heart failure. *J Am Coll Cardiol*. 2013;62(12):1065–1072.
18 Hao P, Jiang F, Cheng J, Ma L, Zhang Y, Zhao Y. Traditional Chinese medicine for cardiovascular disease: evidence and potential mechanisms. *J Am Coll Cardiol*. 2017;69(24):2952–2966.